

Claims

1. A composition for prevention of sclerotic lesions causing apoptosis, degeneration, fibrosis and atrophy and/or for repair
 5 and regeneration of the aforementioned lesions, comprising a compound which preferentially increases regeneration-promoting macrophages.

2. A pharmaceutical for prevention and/or therapy of renal
 10 glomerular lesions, lesions of pancreatic islets of Langerhans or epidermal lesions, comprising a compound which preferentially increases regeneration-promoting CD11b⁺CD2⁺ macrophages.

3. The pharmaceutical as claimed in claim 2, wherein the compound
 15 which preferentially increasing regeneration-promoting CD11b⁺CD2⁺ macrophages is one or more compound(s) selected from the group consisting of (R)-1-naphthalen-2-ylethyl (R)-2-(4-fluorophenoxy)-5-oxotetrahydrofuran-2-carboxylate,
 20 2-fluoro-5-oxotetrahydrofuran-2-carboxylic acid benzyl ester, bacitracin A, viomycin, 6,7-dimethoxy-1-morpholinomethyl-isochromane, 1-diethylaminomethyl-5-butoxy-6-methoxy-1,2,3,4-tetrahydroisoquinoline, 1-(4-fluorophenylthio)-2-
 25 methylaminopropanone, 2-chloro-5-oxotetrahydrofuran-2-carboxylic acid benzyl ester and 1-(2-oxo-hemiglutaric acid) benzyl ester.

4. A pharmaceutical for prevention and/or therapy of renal

tubulointerstitial lesions, lesions of pancreatic exocrine or interstitial tissues, or dermal lesions, comprising a compound which promotes induction of human regeneration-promoting CD11b⁻CD2⁺ macrophages.

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5. The pharmaceutical as claimed in claim 4, wherein the compound promoting induction of regeneration-promoting CD11b⁻CD2⁺ macrophages is one or more compound(s) selected from the group consisting of (R)-1-naphthalen-2-ylethyl (S)-

10 2-(4-fluorophenoxy)-5-oxotetrahydrofuran-2-carboxylate, 2-benzyl-5-oxo-2-tetrahydrofuran carboxylic acid benzyl ester, 1-chloro-3-oxo-1,3-dihydroisobenzofuran-1-carboxylic acid benzyl ester and 1-(2-oxo-hemiglutaric acid) ethyl ester.

15 6. A pharmaceutical for prevention and/or therapy of kidney diseases, pancreatic diseases or skin diseases, comprising the compound described in claim 2 and the compound described in claim 4.

20 7. A pharmaceutical for prevention and/or therapy of kidney diseases, pancreatic diseases or skin diseases, comprising a compound which promotes induction of regeneration-promoting CD11b⁺CD2⁺ macrophages and regeneration-promoting CD11b⁻CD2⁺ macrophages.

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8. The pharmaceutical as claimed in claim 7, wherein the compound promoting induction of regeneration-promoting CD11b⁺CD2⁺ macrophages and regeneration-promoting CD11b⁻CD2⁺ macrophages is one or more compound(s) selected from the group consisting

of 2-(4-chlorophenyl)thio-5-oxo-2-tetrahydrofuran carboxylic acid benzyl ester, 2-(4-fluorophenyl)oxy-5-oxo-2-tetrahydrofurancarboxylic acid ethyl ester, 2-(2,4-difluorophenyl)sulfonyl-5-oxo-2-tetrahydrofurancarboxylic acid benzyl ester, 2-phenoxy-5-oxo-2-tetrahydrofurancarboxylic acid benzhydryl ester, 2-(4-fluorophenyl)thio-5-oxo-2-tetrahydrofuran carboxylic acid, 2-(4-methoxyphenyl)thio-5-oxo-2-tetrahydrofurancarboxylic acid, 2-(2,4-difluorophenyl)thio-5-oxo-2-tetrahydrofurancarboxylic acid and 2-(4-fluorophenyl)sulfonyl-5-oxo-2-tetrahydrofurancarboxylic acid benzyl ester.

9. A cosmetic comprising a compound which promotes induction of regeneration-promoting CD11b⁺CD2⁺ macrophages.

10. The cosmetic as claimed in claim 9, wherein the compound promoting induction of regeneration-promoting CD11b⁺CD2⁺ macrophages is one or more compound(s) selected from the group consisting of (R)-1-naphthalen-2-ylethyl (R)-2-(4-fluorophenoxy)-5-oxotetrahydrofuran-2-carboxylate, 2-fluoro-5-oxotetrahydrofuran-2-carboxylic acid benzyl ester, bacitracin A, viomycin, 6,7-dimethoxy-1-morpholinomethyl-isochromane, 1-diethylaminomethyl-5-butoxy-6-methoxy-1,2,3,4-tetrahydroisoquinoline, 1-(4-fluorophenylthio)-2-methylaminopropanone, 2-chloro-5-oxotetrahydrofuran-2-carboxylic acid benzyl ester

and 1-(2-oxo-hemiglutaric acid) benzyl ester.

11. A cosmetic comprising a compound which promotes induction of regeneration-promoting $CD11b^-CD2^+$ macrophages.

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12. The cosmetic as claimed in claim 11, wherein the compound promoting induction of regeneration-promoting $CD11b^-CD2^+$ macrophages is one or more compound(s) selected from the group consisting of (R)-1-naphthalen-2-ylethyl (S)-2-(4-fluorophenoxy)-5-oxotetrahydrofuran-2-carboxylate, 2-benzyl-5-oxo-2-tetrahydrofurancarboxylic acid benzyl ester, 1-chloro-3-oxo-1,3-dihydroisobenzofuran-1-carboxylic acid benzyl ester and 1-(2-oxo-hemiglutaric acid) ethyl ester.

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13. A cosmetic comprising the compound described in claim 9 and the compound described in claim 11.

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14. A cosmetic comprising a compound which promotes induction of regeneration-promoting $CD11b^+CD2^+$ macrophages and regeneration-promoting $CD11b^-CD2^+$ macrophages.

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15. The cosmetic as claimed in claim 14, wherein the compound promoting induction of regeneration-promoting $CD11b^+CD2^+$ macrophages and regeneration-promoting $CD11b^-CD2^+$ macrophages is one or more compound(s) selected from the group consisting of 2-(4-chlorophenyl)thio-5-oxo-2-tetrahydrofurancarboxylic acid benzyl ester, 2-(4-fluorophenyl)oxy-5-oxo-2-tetrahydrofurancarboxylic acid ethyl ester, 2-(2,4-difluorophenyl)sulfonyl-5-oxo-2-

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tetrahydrofurancarboxylic acid benzyl ester,
 2-phenoxy-5-oxo-2-tetrahydrofurancarboxylic acid benzhydryl
 ester, 2-(4-fluorophenyl)thio-5-oxo-2-tetrahydrofuran
 carboxylic acid, 2-(4-methoxyphenyl)thio-5-oxo-2-
 5 tetrahydrofurancarboxylic acid,
 2-(2,4-difluorophenyl)thio-5-oxo-2-tetrahydrofurancarboxylic
 acid and 2-(4-fluorophenyl)sulfonyl-5-oxo-2-tetrahydrofuran
 carboxylic acid benzyl ester.

10 16. A method for screening a compound which is able to prevent,
 mitigate or treat renal glomerular lesions, lesions of pancreatic
 islets of Langerhans or epidermal lesions, which comprises
 measuring a promoting action of a compound to be tested on the
 induction of regeneration-promoting $CD11b^+CD2^+$
 15 macrophages and regulatory $CD2^-CD4^+$ T lymphocytes caused by
 contact of human peripheral blood mononuclear cells with a
 lipopolysaccharide.

17. A method for screening a compound which is able to prevent,
 20 mitigate or treat renal tubulointerstitial lesions, lesions of
 pancreatic exocrine or interstitial tissues, or dermal lesions,
 which comprises measuring a promoting action of a compound to
 be tested on the induction of regeneration-promoting $CD11b^-CD2^+$
 macrophages and/or regulatory $CD2^-CD4^+$ T lymphocytes caused by
 25 contact of human peripheral blood mononuclear cells with
 mitomycin-treated human peripheral blood mononuclear cells.

18. A kit for screening a compound which is able to prevent,
 mitigate or treat renal glomerular lesions, lesions of pancreatic

islets of Langerhans or epidermal lesions, which comprises (a) human peripheral blood mononuclear cells, (b) lipopolysaccharide and optionally (c) human AB type serum and/or (d) RPMI 1640 medium.

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19. A kit for screening a compound which is able to prevent, mitigate or treat renal tubulointerstitial lesions, lesions of pancreatic exocrine or interstitial tissues, or dermal lesions, which comprises (a) human peripheral blood mononuclear cells, (b) mitomycin-treated human peripheral blood mononuclear cells and optionally (c) human AB type serum and/or (d) RPMI 1640 medium.

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20. A kit for screening a compound which is able to prevent, mitigate or treat dermal lesions, which comprises (a) human peripheral blood mononuclear cells, (b) mitomycin-treated human peripheral blood mononuclear cells and optionally (c) human AB type serum and/or (d) RPMI 1640 medium.

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21. A method for suppression and/or regeneration of sclerotic lesions causing apoptosis, degeneration, fibrosis and atrophy, which comprises administering a compound which preferentially increases regeneration-promoting macrophages to a patient.

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22. A therapeutic method for renal glomerular lesions, lesions of pancreatic islets of Langerhans or epidermal lesions, which comprises administering a pharmaceutical comprising a compound which promotes induction of regeneration-promoting CD11b⁺CD2⁺ macrophages to a patient.

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23. The therapeutic method as claimed in claim 22, wherein the compound which preferentially increases regeneration-promoting CD11b⁺CD2⁺ macrophages is one or more compound(s) selected from the group consisting of (R)-1-naphthalen-2-ylethyl (R)-2-(4-fluorophenoxy)-5-oxotetrahydrofuran-2-carboxylate, 2-fluoro-5-oxotetrahydrofuran-2-carboxylic acid benzyl ester, bacitracin A, viomycin, 6,7-dimethoxy-1-morpholinomethyl-isochromane, 1-diethylaminomethyl-5-butoxy-6-methoxy-1,2,3,4-tetrahydroisoquinoline, 1-(4-fluorophenylthio)-2-methylaminopropanone, 2-chloro-5-oxotetrahydrofuran-2-carboxylic acid benzyl ester and 1-(2-oxo-hemiglutaric acid) benzyl ester.

24. A therapeutic method for renal tubulointerstitial lesions, lesions of pancreatic exocrine or interstitial tissues, or dermal lesions, which comprises administering a pharmaceutical comprising a compound which promotes induction of regeneration-promoting CD11b⁺CD2⁺ macrophages to a patient.

25. The therapeutic method as claimed in claim 24, wherein the compound promoting induction of regeneration-promoting CD11b⁺CD2⁺ macrophages is one or more compound(s) selected from the group consisting of (R)-1-naphthalen-2-ylethyl (S)-2-(4-fluorophenoxy)-5-oxotetrahydrofuran-2-carboxylate, 2-benzyl-5-oxo-2-tetrahydrofuran carboxylic acid benzyl ester, 1-chloro-3-oxo-1,3-dihydroisobenzofuran-1-carboxylic acid benzyl ester and 1-(2-oxo-hemiglutaric acid) ethyl ester.

26. A therapeutic method for kidney diseases, pancreatic diseases or skin diseases, which comprises concurrently administering the pharmaceutical described in claim 22 and the pharmaceutical described in claim 24 to a patient.

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27. A therapeutic method for kidney diseases, pancreatic diseases or skin diseases, which comprises administering a compound which promotes induction of regeneration-promoting CD11b⁺CD2⁺ macrophages and regeneration-promoting CD11b⁻CD2⁺ macrophages to a patient.

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28. The therapeutic method as claimed in claim 27, which comprises concurrently administering a compound promoting induction of regeneration-promoting CD11b⁺CD2⁺ macrophages and a compound promoting induction of regeneration-promoting CD11b⁻CD2⁺ macrophages, each of which being one or more compound(s) selected from the group consisting of 2-(4-chlorophenyl)thio-5-oxo-2-tetrahydrofuran carboxylic acid benzyl ester,

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2-(4-fluorophenyl)oxy-5-oxo-2-tetrahydrofurancarboxylic acid ethyl ester,

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2-(2,4-difluorophenyl)sulfonyl-5-oxo-2-tetrahydrofurancarboxylic acid benzyl ester, 2-phenoxy-5-oxo-2-tetrahydrofurancarboxylic acid benzhydryl ester,

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2-(4-fluorophenyl)thio-5-oxo-2-tetrahydrofurancarboxylic acid,

2-(4-methoxyphenyl)thio-5-oxo-2-tetrahydrofurancarboxylic acid,

2-(2,4-difluorophenyl)thio-5-oxo-2-tetrahydrofurancarboxylic acid and 2-(4-fluorophenyl)sulfonyl-5-oxo-2-tetrahydrofurancarboxylic acid benzyl ester, to a patient.

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29. Use of a compound which preferentially increases regeneration-promoting macrophages for production of a pharmaceutical which suppresses and/or regenerates sclerotic lesions causing apoptosis, degeneration, fibrosis and atrophy.

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30. Use of a compound which promotes induction of regeneration-promoting CD11b⁺CD2⁺ macrophages for production of a pharmaceutical which prevents and/or treats renal glomerular lesions, lesions of pancreatic islets of Langerhans or epidermal lesions.

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31. Use of a compound which promotes induction of regeneration-promoting CD11b⁺CD2⁺ macrophages for production of a cosmetic.

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32. The use as claimed in claim 30 or claim 31, wherein the compound preferentially increasing regeneration-promoting CD11b⁺CD2⁺ macrophages is one or more compound(s) selected from the group consisting of (R)-1-naphthalen-2-ylethyl (R)-2-(4-fluorophenoxy)-5-oxotetrahydrofuran-2-carboxylate, 2-fluoro-5-oxotetrahydrofuran-2-carboxylic acid benzyl ester, bacitracin A, viomycin, 6,7-dimethoxy-1-morpholinomethyl-isochromane, 1-diethylaminomethyl-5-butoxy-6-methoxy-1,2,3,4-

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tetrahydroisoquinoline,
 1-(4-fluorophenylthio)-2-methylaminopropanone,
 2-chloro-5-oxotetrahydrofuran-2-carboxylic acid benzyl ester
 and 1-(2-oxo-hemiglutaric acid) benzyl ester.

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33. Use of a compound which promotes induction of
 regeneration-promoting $CD11b^-CD2^+$ macrophages for production
 of a pharmaceutical which prevents or treats renal
 tubulointerstitial lesions, lesions of pancreatic exocrine or
 10 interstitial tissues, or dermal lesions.

34. Use of a compound which promotes induction of
 regeneration-promoting $CD11b^-CD2^+$ macrophages for production
 of a cosmetic.

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35. The use as claimed in claim 33 or claim 34, wherein the
 compound promoting induction of regeneration-promoting
 $CD11b^-CD2^+$ macrophages is one or more compound(s) selected from
 the group consisting of (R)-1-naphthalen-2-ylethyl
 20 (S)-2-(4-fluorophenoxy)-5-oxotetrahydrofuran-2-carboxylate,
 2-benzyl-5-oxo-2-tetrahydrofurancarboxylic acid benzyl ester,
 1-chloro-3-oxo-1,3-dihydroisobenzofuran-1-carboxylic acid
 benzyl ester and 1-(2-oxo-hemiglutaric acid) ethyl ester.

25 36. Use of a compound which promotes induction of
 regeneration-promoting $CD11b^+CD2^+$ macrophages and
 regeneration-promoting $CD11b^-CD2^+$ macrophages for production
 of a pharmaceutical which prevents or treats kidney diseases,
 pancreatic diseases or skin diseases.

37. Use of a compound which promotes induction of
 regeneration-promoting $CD11b^+CD2^+$ macrophages and
 regeneration-promoting $CD11b^-CD2^+$ macrophages for production
 5 of a cosmetic.

38. The therapeutic method as claimed in claim 36 or claim 37,
 wherein the compound promoting induction of
 regeneration-promoting $CD11b^+CD2^+$ macrophages and
 10 regeneration-promoting $CD11b^-CD2^+$ macrophages is one or more
 compound(s) selected from the group consisting of
 2-(4-chlorophenyl)thio-5-oxo-2-tetrahydrofurancarboxylic
 acid benzyl ester (III-1),
 2-(4-fluorophenyl)oxy-5-oxo-2-tetrahydrofurancarboxylic
 15 acid ethyl ester (III-2),
 2-(2,4-difluorophenyl)sulfonyl-5-oxo-2-
 tetrahydrofurancarboxylic acid benzyl ester,
 2-phenoxy-5-oxo-2-tetrahydrofurancarboxylic acid benzhydryl
 ester,
 20 2-(4-fluorophenyl)thio-5-oxo-2-tetrahydrofurancarboxylic
 acid,
 2-(4-methoxyphenyl)thio-5-oxo-2-tetrahydrofurancarboxylic
 acid,
 2-(2,4-difluorophenyl)thio-5-oxo-2-
 25 tetrahydrofurancarboxylic acid and
 2-(4-fluorophenyl)sulfonyl-5-oxo-2-
 tetrahydrofurancarboxylic acid benzyl ester.